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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,362	07/09/2001	Stafford McLean	PC10782A	5342

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EXAMINER
KIM, VICKIE Y

ART UNIT	PAPER NUMBER
1614	//

DATE MAILED: 09/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/901,362	Applicant(s) MCLEAN ET AL.	
	Examiner Vickie Kim	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *3-8 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application

1. The elected claims 1-2 and 9 are presented for the examination. There is typographical error found in the previous office action. This examiner made several attempts to inform the applicant and try to resolve without issuing supplemental office action to expedite the prosecution. However, the examiner has failed to communicate to applicant's representative in the time allowed where the issuance of the instant written supplemental office action is necessary to avoid further delay. The instant supplemental office action supercedes any previous office actions of the record.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-2 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO98/52565(Yale Univ.) and US6,001,848(Noble) in view of and US 6,444,679 (Liras et al).

The instant claims are directed to a method for treating chemical dependency by using a combination of delta opioid receptor ligand(e.g. compound of formula I) and a serotonin reuptake inhibitor(e.g.sertraline).

WO'565 teaches a combination drug therapy for treating chemical dependency(e.g. alcoholism) wherein the combination comprises an effective amount of

an opioid antagonist (e.g. naloxone or naltrexone) and a serotonin reuptake inhibitor(e.g. sertraline), see abstract. It contemplates an example of a drug therapy for treating alcohol dependence using a combination of sertraline and naltrexone at page 12, example 1. It further teaches that the said combination drug enhances the effectiveness while it decreases the side effects associated with the opioid antagonist, see abstract.

US'848 also teaches a treatment for alcoholism using a dopamine agonist(i.e. bromocriptine) or opioids. Furthermore, US'848 teaches the alternative therapeutic modality, the administration of opioidergic compounds(e.g. naloxone or naltrexone) in combination with one or more serotonin reuptake inhibitor such as sertraline, see column 7, lines 55-45. However, the teaching of US'848 is particularly pertinent to the instant claims because it teaches the involvement of delta opioid receptor in chronic ethanol exposure(alcoholism). For instance, chronic ethanol exposure enhanced delta opiate binding in the brain so that naloxone which is only binds to delta opioid receptor at high concentration, binds to the delta opiate receptor not necessarily at high concentration, for example, naloxone shows the binding activity at 1.15nM to not only mu(μ) but also delta(δ)binding site in alcoholism. It elucidates the delta opioid receptor involvement and the underlying mechanism wherefrom the therapeutic effectiveness of naloxone against chemical dependency(i.e. alcoholism) is derived(see column 26, lines 45-60).

Thus, when these references(WO'565 and US'848) are combined together, one would have been conclude that the drug combination of naloxone(delta opioid receptor

ligand in the case of chronic ethanol exposure) and serotonic reuptake inhibitor such as sertraline is effectively used in the treatment of the chemical dependency.

Applicant's claims are still different because they require specific compound having the formula I(elected species) as the delta opioid receptor ligand instead of naloxone.

However, it would have been obvious to one of ordinary skill in the art at that time of the invention was made to substitute naloxone(of WO'565 and US'848) with a selective delta opioid ligand such as a compound having the formula I when WO'565 and US'848(combined) is taken in view of US'605 because the references together remedy the deficiency found in WO'565 and US'848 combined.

US'679 teaches a selective delta opioid receptor ligands including the elected species (compound of the formula I) and its use in the treatment of chemical dependency including alcoholism, see column 2, lines 46-66 and claims 1-5. It further teaches that these selective delta opioid compounds are particularly effective without the side effects of conventionally known non-selective opiates such as morphine.

When these references are take together(WO'565 and US'848 in view of US'679), one would have been motivated to make such modification to enhance the therapeutic efficacy by substituting non selective delta opioid receptor ligand with selective delta receptor ligand so that the therapeutic end result would be maximized while unwanted side effect associate with non-selective opioids could be reduced. It is conventional practice to modify therapeutic modalities to alternate single therapy with combination drug therapy to enhance the efficacy while lowering the dose of each active

component and reducing unwanted side effect that is usually associated with higher dose used or related to particular component since each component used in the drug combination therapy utilizes two different bio-pathways. Thus, one would have expected the achievement of better therapeutic outcome with least unwanted side-effects by said substitution and the replacement of non-selective opioid ligand with the selective opioid ligand without undue experiment and thus, obvious absent evidence to the contrary.

One would have been motivated to do so with reasonable expectation of success because the superiority and the effectiveness of the selective delta opioid receptor ligand, the claimed compound having the formula I in this case, and the drug combination therapy has been proven and well suggested in the cited references.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same (or similar) ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-2 and 9 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-6 of U.S. Patent No. 6,444,679 in view of WO98/52565. As mentioned immediately abouve in 103 rejection (sdupra) US'679 teaches a delta opioid receptor ligand (e.g. 4-phenyl-4-heteroarylpiperidine derivatives whith the formula I) used in the treatment of chemical dependency, see claims 1 and 5-6.

Applicant's claims differ because they require serotonin reuptake inhibitor(sertraline). However, it would have been obvious to one of ordinary skill in the art to add sertraline to enhance therapeutic efficacy because sertraline is already known as an effective drug for treating chemical dependency. Additionally, the combination drug therapy using a serotonin reuptake inhibitor and an opioid compound are also conventional known at the time of the invention made as evidenced WO565 patent. WO'565 teaches serotonin reiptake inhibitor(i.e. sertraline) is effectively used in the treatment of chemical dependency including alcoholism. WO'565 uses non-selective opioid such as naloxone or naltrexone in the combination therapy. Thus, one would have been motivated to substitute the said non-selective opioid with selective delta-opioid receptor ligand to enhance the therapeutic efficacy by increasing the effectiveness while reducing the side effects associated with non-selective opioids. It is well known practice in the art that adding secondary beneficial agent to lower the dose of each component so that undesirable side effects could be reduced while maintaining

the therapeutic effectiveness by utilizing different underlying mechanism. Thus, one would have been motivated to do so with reasonable expectation of success because the delta opioid receptor ligands are selectively binds to the delta receptor without the side effects and the delta opioid receptor is particularly related to the chemical dependency and thus, the combination of delta opioid receptor ligand and sertraline(serotonin reuptake inhibitor) would maximize its effectiveness wile least side effects could be expected.

Conclusion

5. No claim is allowed.

6. Applicants arguments are moot in the view of new ground of rejections.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Vickie Kim,
Patent examiner

August 29, 2003
Art unit 1614